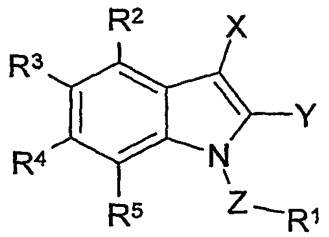
Claims

1. A compound of formula I,



I

wherein X represents an optionally substituted aryl or heteroaryl group or an optionally substituted amide, amine or sulfonamide group, which latter three groups are connected to the indole ring through their nitrogen atom;

Y represents a carboxylic acid, a carboxylic acid ester, a carboxylic acid amide, a hydroxamic acid, a hydroxamic acid ester or hydroxymethyl;

Z represents a spacer group;

R^1 represents an optionally substituted aryl or heteroaryl group;

one of the groups R^2, R^3, R^4 and R^5 represents an optionally substituted aryl or heteroaryl group.

2. A compound as claimed in Claim 1; wherein:

X represents:

i) an aryl group or a heteroaryl group, both of which groups are optionally substituted by one or more substituents selected from A; or

ii) $-N(R^6)-E-R^7$;

E represents a single bond, –C(O)- or –$S(O)_n$-;

Y represents $–CH_2OH$, -C(O)N(H)R^8, -C(O)N(H)OR^8 or –C(O)OR^8;

Z represents a C_{1-8} alkylene or a C_{2-8} heteroalkylene chain, both of which:

(i) optionally contain one or more unsaturations;

(ii) are optionally substituted by one or more substituents selected from halo, -R^8, -N(R^8)(R^9), -OR^8 and =O; and/or

(iii) may form part of an additional 3- to 8-membered ring formed between any one or more members of the C_{1-8} alkylene or C_{2-8} heteroalkylene chain, which ring optionally contains 1 to 3 heteroatoms and/or 1 to 3 unsaturations and which ring is itself optionally substituted by one or more substituents selected from halo, -R^8, –N(R^8)(R^9), -OR^8 and =O;

R^1 represents an aryl or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from A;

one of the groups R^2, R^3, R^4 and R^5 represents an aryl group or a heteroaryl group (both of which are optionally substituted by one or more substituents selected from A) and:

a) the other groups are independently selected from hydrogen, G^1, an aryl group, a heteroaryl group (which latter two groups are optionally substituted by one or more substituents selected from A), C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl (which latter five groups are optionally substituted by one or more substituents selected from G^1 and/or Q^1); and/or

b) any two other groups which are adjacent to each other are optionally linked to form, along with two atoms of the essential benzene ring in the compound of formula I, a 5- to 6-membered ring, optionally containing 1 or

more heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from halo, $-R^8$, $-OR^8$ and =O;

A represents, on each occasion when mentioned above:

I) an aryl group or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from B;

II) a C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl group, all of which are optionally substituted by one or more substituents selected from G^1 and/or Q^1; or

III) a G^1 group; or

IV) two adjacent A substituents may be linked together to form, along with the essential atoms of the aryl or heteroaryl group to which the two A substituents are attached, a further 5- to 6-membered ring, optionally containing 1 or more heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from halo, $-R^8$, $-OR^8$ and =O;

G^1 represents, on each occasion when mentioned above, halo, cyano, $-N_3$, $-NO_2$, $-ONO_2$ or $-A^1-R^{10}$;

wherein A^1 represents a single bond or a spacer group selected from $-C(Q^2)A^2-$, $-S(O)_nA^3-$, $-N(R^{11})A^4-$, $-OA^5-$ and –S-, in which:

A^2 represents A^6 or –S-;

A^3 represents A^6;

A^4 represents A^7, $-C(Q^2)N(R^{11})C(Q^2)N(R^{11})-$, $-C(Q^2)N(R^{11})C(Q^2)O-$, $-C(Q^2)N(R^{11})S(O)_nN(R^{11})-$, $-C(Q^2)S-$, $-S(O)_nN(R^{11})C(Q^2)N(R^{11})-$, $-S(O)_nN(R^{11})C(Q^2)O-$, $-S(O)_nN(R^{11})S(O)_nN(R^{11})-$ or $-S(O)_nO-$;

A^5 represents A^7 or $-S(O)_nO-$;

A^6 represents a single bond, $-N(R^{11})-$ or –O-;

A^7 represents a single bond, $-C(Q^2)-$, $-C(Q^2)N(R^{11})-$, $-C(Q^2)O-$, $-S(O)_n-$ or $-S(O)_nN(R^{11})$;

Q^1 and Q^2 independently represent, on each occasion when mentioned above, =O, =S, $=NR^{10}$, $=NN(R^{10})(R^{11})$, $=NOR^{10}$, $=NS(O)_2N(R^{10})(R^{11})$, =NCN, $=C(H)NO_2$ or $=C(R^{10})(R^{11})$;

R^6 and R^7 independently represent, on each occasion when mentioned above:

I) hydrogen;

II) an aryl group or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from B; or

III) a C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl group, all of which groups are optionally substituted by one or more substituents selected from G^2 and/or Q^3; or

R^6 and R^7 may be linked together to form along with the N atom and –E- group to which R^6 and R^7 are respectively attached, a 5- to 8-membered ring, optionally containing 1 to 3 heteroatoms and/or 1 to 3 unsaturations, which ring is optionally substituted by one or more substituents selected from G^2 and/or Q^3;

B represents, on each occasion when mentioned above:

I) an aryl group or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from G^2 and/or wherein any two adjacent atoms of the aryl or heteroaryl group may be linked together to form a further 5- to 6-membered ring, optionally containing 1 or more heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from halo, $-R^8$, $-OR^8$ and =O;

II) a C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl group, all of which are optionally substituted by one or more substituents selected from G^2 and/or Q^3; or

III) a G^2 group; or

IV) two adjacent B substituents may be linked together to form, along with the essential atoms of the aryl or heteroaryl group to which the two B substituents are attached, a further 5- to 6-membered ring, optionally containing 1 or more heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from halo, $-R^8$, $-OR^8$ and =O;

G^2 represents, on each occasion when mentioned above, halo, cyano, $-N_3$, $-NO_2$, $-ONO_2$ or $-A^8-R^{12}$;

wherein A^8 represents a single bond or a spacer group selected from $-C(Q^4)A^9-$, $-S(O)_nA^{10}-$, $-N(R^{13})A^{11}-$, $-OA^{12}-$ and –S-, in which:

A^9 represents A^{13} or –S-;

A^{10} represents A^{13};

A^{11} represents A^{14}, $-C(Q^4)N(R^{13})C(Q^4)N(R^{13})-$, $-C(Q^4)N(R^{13})C(Q^4)O-$, $-C(Q^4)N(R^{13})S(O)_nN(R^{13})-$, $-C(Q^4)S-$, $-S(O)_nN(R^{13})C(Q^4)N(R^{13})-$, $-S(O)_nN(R^{13})C(Q^4)O-$, $-S(O)_nN(R^{13})S(O)_nN(R^{13})-$ or $-S(O)_nO-$;

A^{12} represents A^{14} or $-S(O)_nO-$;

A^{13} represents a single bond, $-N(R^{13})-$ or –O-;

A^{14} represents a single bond, $-C(Q^4)-$, $-C(Q^4)N(R^{13})-$, $-C(Q^4)O-$, $-S(O)_n-$ or $-S(O)_nN(R^{13})$;

Q^3 and Q^4 independently represent, on each occasion when mentioned above, =O, =S, $=NR^{12}$, $=NN(R^{12})(R^{13})$, $=NOR^{12}$, $=NS(O)_2N(R^{12})(R^{13})$, =NCN, $=C(H)NO_2$ or $=C(R^{12})(R^{13})$;

R^8, R^9, R^{10}, R^{11}, R^{12} and R^{13} are independently selected from:

i) hydrogen;

ii) an aryl or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from G^3 and/or wherein any two adjacent atoms of the aryl or heteroaryl group may be linked together to form a further 5- to 6-membered ring, optionally containing 1 or more heteroatoms, which ring is itself optionally substituted by one or more substituents selected from halo, $-R^{14}$, $-OR^{14}$ and =O; or

iii) a C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl group, all of which are optionally substituted by one or more substituents selected from G^3 and/or W^1; or

any pair of R^8, R^9, R^{10}, R^{11}, R^{12} and R^{13} may, for example when present on the same or on adjacent atoms, be linked together to form with those, or other relevant, atoms, a further 5- to 8-membered ring, optionally containing 1 to 3 heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from G^3 and/or W^1;

G^3 represents, on each occasion when mentioned above, halo, cyano, $-N_3$, $-NO_2$, $-ONO_2$ or $-A^{15}-R^{15}$;

wherein A^{15} represents a single bond or a spacer group selected from $-C(W^2)A^{16}-$, $-S(O)_nA^{17}-$, $-N(R^{16})A^{18}-$, $-OA^{19}-$ and $-S-$, in which:

A^{16} represents A^{20} or $-S-$;

A^{17} represents A^{20};

A^{18} represents A^{21}, $-C(W^2)N(R^{16})C(W^2)N(R^{16})-$, $-C(W^2)N(R^{16})C(W^2)O-$, $-C(W^2)N(R^{16})S(O)_nN(R^{16})-$, $-C(W^2)S-$, $-S(O)_nN(R^{16})C(W^2)N(R^{16})-$, $-S(O)_nN(R^{16})C(W^2)O-$, $-S(O)_nN(R^{16})S(O)_nN(R^{16})-$ or $-S(O)_nO-$;

A^{19} represents A^{21} or $-S(O)_nO-$;

A^{20} represents a single bond, $-N(R^{16})-$ or $-O-$;

A^{21} represents a single bond, $-C(W^2)-$, $-C(W^2)N(R^{16})-$, $-C(W^2)O-$, $-S(O)_n-$ or $-S(O)_nN(R^{16})$;

W^1 and W^2 independently represent, on each occasion when mentioned above, =O, =S, $=NR^{15}$, $=NN(R^{15})(R^{16})$, $=NOR^{15}$, $=NS(O)_2N(R^{15})(R^{16})$, =NCN, $=C(H)NO_2$ or $=C(R^{15})(R^{16})$;

R^{14}, R^{15} and R^{16} are independently selected from:

i) hydrogen;

ii) an aryl or a heteroaryl group, both of which are optionally substituted by one or more substituents selected from G^4, methylenedioxy, difluoromethylenedioxy and/or dimethylmethylenedioxy; or

iii) a C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl or C_{3-8} heterocycloalkyl group, all of which are optionally substituted by one or more substituents selected from G^4 and/or J; or

any pair of R^{14}, R^{15} and R^{16} may, for example when present on the same or on adjacent atoms, be linked together to form with those, or other relevant, atoms, a further 5- to 7-membered ring, optionally containing 1 to 3 heteroatoms and/or 1 to 3 unsaturations, which ring is itself optionally substituted by one or more substituents selected from G^4 and J;

G^4 represents, on each occasion when mentioned above, halo, cyano, $-N_3$, $-NO_2$, $-ONO_2$ or $-A^{22}-R^{17}$;

wherein A^{22} represents a single bond or a spacer group selected from $-C(O)A^{23}-$, $-S(O)_nA^{24}-$, $-N(R^{18})A^{25}-$, $-OA^{26}-$ and –S-, in which:

A^{23} represents A^{27} or –S-;

A^{24} represents A^{27};

A^{25} represents A^{28}, $-C(O)N(R^{18})C(O)N(R^{18})-$, $-C(O)N(R^{18})C(O)O-$, $-C(O)N(R^{18})S(O)_nN(R^{18})-$, $-C(O)S-$, $-S(O)_nN(R^{18})C(O)N(R^{18})-$, $-S(O)_nN(R^{18})C(O)O-$, $-S(O)_nN(R^{18})S(O)_nN(R^{18})-$ or $-S(O)_nO-$;

A^{26} represents A^{28} or $-S(O)_nO-$;

A^{27} represents a single bond, $-N(R^{18})-$ or –O-;

A^{28} represents a single bond, -C(O)-, -C(O)N(R^{18})-, -C(O)O-, -S(O)$_n$- or –S(O)$_n$N(R^{18});

J represents, on each occasion when mentioned above, =O, =S, =NR^{17}, =NN(R^{17})(R^{18}), =NOR^{17}, =NS(O)$_2$N(R^{17})(R^{18}), =NCN, =C(H)NO_2 or =C(R^{17})(R^{18});

R^{17} and R^{18} are independently selected from hydrogen and C_{1-6} alkyl, which latter group is optionally substituted by one or more substituents selected from halo, -NH_2, -N(H)Me, -N(H)Et, -N(H)*i*-Pr, -NMe_2, -N(Me)Et, -N(Me)*i*-Pr, -NEt_2, -OH, -OMe, -OEt, -O*i*-Pr and =O; and

n represents, on each occasion when mentioned above, 1 or 2,

or a pharmaceutically-acceptable salt thereof.

3. A compound as claimed in Claim 2, wherein n represents 2.

4. A compound as claimed in Claim 2 or Claim 3, wherein A represents G^1 or any two adjacent A substituents may be linked by a methylenedioxy group.

5. A compound as claimed in any one of Claims 2 to 4, wherein G^1 represents halo, cyano, -NO_2 or –A^1-R^{10}.

6. A compound as claimed in any one of Claims 2 to 5, wherein A^2 represents A^6.

7. A compound as claimed in any one of Claims 2 to 6, wherein A^3 and A^5 independently represent a single bond.

8. A compound as claimed in any one of Claims 2 to 7, wherein A^4 represents a single bond, $-C(Q^2)-$ or $-S(O)_2-$.

9. A compound as claimed in any one of Claims 2 to 8, wherein Q^2 represents =O.

10. A compound as claimed in any one of Claims 2 to 9, wherein B represents G^2.

11. A compound as claimed in any one of Claims 2 to 10, wherein G^2 represents halo, cyano, $-NO_2$ or $-A^8-R^{12}$.

12. A compound as claimed in any one of Claims 2 to 11, wherein A^8 represents a single bond, $-N(R^{13})A^{11}-$ or $-OA^{12}-$.

13. A compound as claimed in any one of Claims 2 to 12, wherein A^{11} and A^{12} independently represent a single bond.

14. A compound as claimed in any one of the preceding claims, wherein Z represents C_{1-6} alkylene, in which one of the carbon atoms in the chain may be replaced with oxygen.

15. A compound as claimed in any one of the preceding claims, wherein Y represents $-CH_2OH$, $-C(O)NHR^8$ or $-C(O)OR^8$.

16. A compound as claimed in any one of the preceding claims, wherein R^1 represents optionally substituted fluorenyl, phenyl or pyridyl.

17. A compound as claimed in any one of the preceding claims, wherein (when X represents an optionally substituted aryl or heteroaryl group) X represents an optionally substituted phenyl, thienyl, pyridyl, pyrazolyl, pyrazinyl or quinolinyl group.

18. A compound as claimed in any one of the preceding claims, wherein (when they represent an optionally substituted aryl or heteroaryl group) R^2, R^3, R^4 and R^5 represent optionally substituted phenyl, pyridyl or naphthyl.

19. A compound as claimed in Claim 18, wherein the other substituents on the benzene ring of the indole represent hydrogen or G^1.

20. A compound as claimed in any one of Claims 2 to 19, wherein R^6 represents hydrogen or C_{1-3} alkyl group (which latter group is optionally substituted by G^2).

21. A compound as claimed in any one of Claims 2 to 20, wherein R^7 represents phenyl or pyridyl (which groups are optionally substituted by one or more substituents selected from B), or C_{1-4} alkyl, C_{2-4} alkenyl or C_{5-10} cycloalkyl (which latter three groups are optionally substituted by one or more substituents selected from G^2).

22. A compound as claimed in any one of Claims 2 to 19, wherein R^6 and R^7 are linked to form a 5- to 6-membered ring optionally substituted by =O.

23. A compound as claimed in any one of Claims 2 to 22, wherein R^8 and R^{13} independently represent C_{1-3} alkyl or hydrogen.

24. A compound as claimed in any one of Claims 2 to 23, wherein R^{10} represents hydrogen, phenyl, tetrazolyl, C_{1-4} alkyl, C_{2-4} alkenyl or C_{5-6} cycloalkyl, which latter five groups are optionally substituted by one or more substituents selected from G^3.

25. A compound as claimed in any one of Claims 2 to 24, wherein R^{12} represents hydrogen, phenyl, pyrrolyl, C_{1-4} alkyl or C_{5-10} cycloalkyl, which latter four groups are optionally substituted by one or more substituents selected from G^3.

26. A compound as claimed in any one of Claims 2 to 25, wherein R^{11} represents hydrogen or C_{2-4} alkenyl.

27. A compound as claimed in any one of Claims 2 to 26, wherein G^3 represents halo, $-R^{15}$ or $-OR^{15}$.

28. A compound as claimed in any one of Claims 2 to 27, wherein R^{15} represents hydrogen, C_{1-3} alkyl or phenyl.

29. A compound as claimed in any one of Claim 16 to 21, wherein the optional substituents are selected from halo, $-NO_2$, cyano, methylenedioxy, C_{1-6} alkyl (which alkyl group is optionally substituted by one or more substituents selected from a halo group, a phenyl group and OR^{19}), C_{2-6} alkenyl, C_{3-10} cycloalkyl (which cycloalkyl group is optionally substituted with C_{1-6} alkyl), phenyl (which group is optionally substituted with one or more substituents selected from halo and OR^{19}), a heteroaryl group selected from tetrazolyl and pyrrolyl (which groups are optionally substituted by one or more C_{1-6} alkyl groups), methylthio, methylsulfinyl, methylsulfonyl, =O, $-OR^{19}$, $-N(R^{19})R^{20}$, $-C(O)OR^{19}$, $-C(O)R^{19}$, $-C(O)N(R^{19})R^{20}$, $-S(O)_2N(R^{19})R^{20}$ and/or $-N(R^{19})S(O)_2R^{21}$, wherein R^{19} and R^{20}

independently represent hydrogen, phenyl, C_{1-4} alkenyl, C_{1-6} alkyl (which alkyl group is optionally substituted by one or more fluoro atoms) or a phenyl group and R^{21} represents phenyl or C_{1-6} alkyl (which alkyl group is optionally substituted by one or more fluoro atoms).

30. A compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, for use as a pharmaceutical.

31. A pharmaceutical formulation including a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

32. The use of a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, for the manufacture of a medicament for the treatment of a disease in which inhibition of the activity of microsomal prostaglandin E synthase-1 is desired and/or required.

33. A use as claimed in Claim 32, wherein the disease is inflammation.

34. A use as claimed in Claim 33 wherein the disease is inflammatory bowel disease, irritable bowel syndrome, migraine, headache, low back pain, fibromyalgia, a myofascial disorder, a viral infection, a bacterial infection, a fungal infection, dysmenorrhea, a burn, a surgical or dental procedure, a malignancy, atherosclerosis, gout, arthritis, osteoarthritis, juvenile arthritis, rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes, a neurodegenerative disorder, an autoimmune disease, osteoporosis, asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, an allergic disorder, rhinitis, an ulcer, coronary

heart disease, sarcoidosis or any other disease with an inflammatory component.

35. A method of treatment of a disease in which inhibition of the activity of mPGES-1 is desired and/or required, which method comprises administration of a therapeutically effective amount of a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, to a patient suffering from, or susceptible to, such a condition.

36. A combination product comprising:

(A) a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof; and

(B) another therapeutic agent that is useful in the treatment of inflammation,

wherein each of components (A) and (B) is formulated in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

37. A combination product as claimed in Claim 36 which comprises a pharmaceutical formulation including a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, another therapeutic agent that is useful in the treatment of inflammation, and a pharmaceutically-acceptable adjuvant, diluent or carrier.

38. A combination product as claimed in Claim 36 which comprises a kit of parts comprising components:

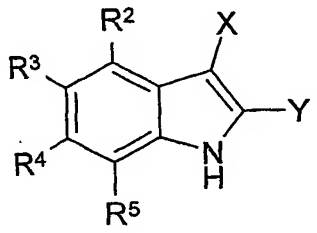
(a) a pharmaceutical formulation including a compound as defined in any one of Claims 1 to 29, or a pharmaceutically-acceptable salt thereof, in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier; and

(b) a pharmaceutical formulation including another therapeutic agent that is useful in the treatment of inflammation in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier,

which components (a) and (b) are each provided in a form that is suitable for administration in conjunction with the other.

39. A process for the preparation of a compound as defined in Claim 2, which comprises:

(i) reaction of a compound of formula II,



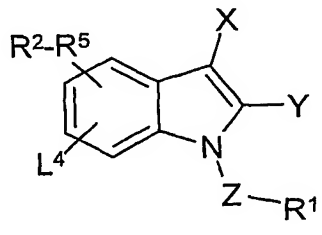
II

wherein X, Y, R^2, R^3, R^4 and R^5 are as defined in Claim 2, with a compound of formula III,

$$R^1ZL^1 \qquad \text{III}$$

wherein L^1 represents a suitable leaving group and R^1 and Z are as defined in Claim 2;

(ii) reaction of a compound of formula IV,



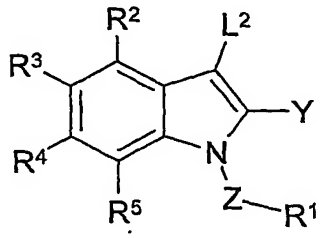
IV

wherein L^4 represents L^2 or L^3, in which L^2 and L^3 represent appropriate leaving groups and L^4 is attached to one or more of the carbon atoms of the benzenoid ring of the indole, and the remaining positions of the benzenoid ring are substituted with 1 to 3 (depending on the number of L^4 substituents) substituents R^2 to R^5 as appropriate, and Z, X, Y, R^1, R^2, R^3, R^4 and R^5 are as defined in Claim 2, with a compound of formula V,

$$R^{22}L^5 \qquad V$$

wherein R^{22} represents R^2, R^3, R^4 or R^5 (as appropriate), and L^5 represents L^2 (when L^4 is L^3) or L^3 (when L^4 is L^2) as defined above;

(iii) for compounds of formula I in which X represents an optionally substituted aryl or heteroaryl group, reaction of a compound of formula VI,



VI

wherein L^2 is as defined above and Z, Y, R^1, R^2, R^3, R^4 and R^5 are as defined in Claim 2, with a compound of formula VII,

$$X^aL^3 \qquad VII$$

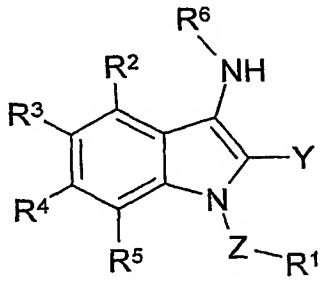
wherein L^3 is as defined above and X^a represents an aryl or heteroaryl group, optionally substituted as defined in Claim 2;

(iv) for compounds of formula I in which X represents $-N(R^6)-E-R^7$, reaction of a compound of formula VI as defined above, with a compound of formula VIII,

$HN(R^6)\text{-}E\text{-}R^7$ VIII

wherein E, R^6 and R^7 are as defined in Claim 2;

(v) for compounds of formula I in which X represents $-N(R^6)\text{-}E\text{-}R^7$, reaction of a compound of formula IX,



IX

wherein Z, Y, R^1, R^2, R^3, R^4, R^5 and R^6 are as defined in Claim 2, with a compound of formula X,

$R^7\text{-}E\text{-}L^1$ X

wherein L^1 is as defined above and E and R^7 are as defined in Claim 2;

(vi) for compounds of formula I in which E represents a single bond and R^7 is a $C_{1\text{-}6}$ alkyl group, $C_{3\text{-}6}$ alkenyl or a $C_{3\text{-}6}$ alkynyl group, reduction of a compound of formula I, wherein X represents –C(O)- and R^7 represents H, a $C_{1\text{-}5}$ alkyl group, a $C_{2\text{-}5}$ alkenyl or a $C_{2\text{-}5}$ alkynyl group.